

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
15 September 2005 (15.09.2005)

PCT

(10) International Publication Number  
**WO 2005/085196 A3**

(51) International Patent Classification<sup>7</sup>: **C07D 209/48**,  
233/66, 471/04, A61K 31/4035, A61P 35/00

(21) International Application Number:  
PCT/EP2005/002437

(22) International Filing Date: 8 March 2005 (08.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
04005498.3 8 March 2004 (08.03.2004) EP  
04014619.3 22 June 2004 (22.06.2004) EP

(71) Applicants (for all designated States except US): **DKFZ** [DE/DE]; Deutsches Krebsforschungszentrum, Stiftung des öffentlichen Rechts, Im Neuenheimer Feld 280, 69120 Heidelberg (DE). **INSTITUTE OF BIOCHEMISTRY AND BIOPHYSICS PAS** [PL/PL]; Pawinskiego 5a, 02-106 Warszawa (PL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GARCIA BOY, Regine** [DE/DE]; Mönchhofstrasse 54, 69120 Heidelberg (DE). **LYKO, Frank** [DE/DE]; Albert-Mays-Strasse 3, 69115 Heidelberg (DE). **SIEDLECKI, Pawel** [PL/PL]; Mokotowska 24/4, PL-00-560 Warsaw (PL).

(74) Agent: **HUHN, Michael**; Isenbruck, Bösl, Hörschler, Wichmann, Huhn, Patentanwälte, Theodor-Heuss-Anlage 12, 68165 Mannheim (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

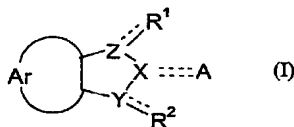
**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
8 December 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: INHIBITORS OF DNA METHYLATION IN TUMOR CELLS



(57) Abstract: The present invention relates to compounds according to the general formula (I) wherein the dotted lines denote a single bond which is optionally present, with 2 dotted lines denoting a double bond; wherein, in case no double bond is present and a free valence exists, this valence is occupied by H; and wherein the symbols in particular have the following meanings: R<sup>1</sup> and R<sup>2</sup> are independently from each other selected from the group consisting of: H; OH; (=O); halogens; pseudohalogens; NH<sub>2</sub>; S(O)<sub>m</sub>R<sup>5</sup>; SO<sub>2</sub>NH<sub>2</sub>; C(O)R<sup>8</sup>; C(O)OR<sup>9</sup>; CONH<sub>2</sub>; C<sub>1</sub>-C<sub>2</sub>-alkyl substituted by NH<sub>2</sub>, OH, S(O)<sub>m</sub>R<sup>5</sup>, SO<sub>2</sub>NH<sub>2</sub>, C(O)R<sup>8</sup>, C(O)OR<sup>9</sup>, CONH<sub>2</sub>; C<sub>1</sub>-C<sub>2</sub>-alkoxy substituted by NH<sub>2</sub>, OH, S(O)<sub>m</sub>R<sup>5</sup>, SO<sub>2</sub>NH<sub>2</sub>, C(O)R<sup>8</sup>, C(O)OR<sup>9</sup>, CONH<sub>2</sub>; Ar denotes an unsubstituted mononuclear aryl group having 6 or 7 members, which aryl group is annulated to the neighbouring 5-membered cycle, and which may carry 1, 2 or 3 heteroatoms from the group N, O and S in its cycle; Y, Z denote independently from each other a nitrogen atom or a methylene group; X is a nitrogen atom or a methylene group; A is selected from the group consisting of: H; halogens and pseudohalogens; OH; =N(OH); NR<sup>12</sup>R<sup>13</sup>; OSO<sub>3</sub>; S(O)<sub>m</sub>R<sup>14</sup>; SO<sub>2</sub>NR<sup>15</sup>R<sup>16</sup>; C(O)R<sup>17</sup>; C(O)OR<sup>18</sup>; CONR<sup>19</sup>R<sup>20</sup>; C(S)R<sup>21</sup>; C(S)OR<sup>22</sup>; unsubstituted and at least monosubstituted C<sub>1</sub>-C<sub>6</sub>-alkyl which can carry in its chain one or more non-adjacent heteroatoms from the group nitrogen and oxygen. These compounds are used as inhibitors of DNA methylation and therefore useful in the treatment of various forms of cancer.



WO 2005/085196 A3